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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,276	08/27/1999	HIDEAKI TADA	Q55589	2406

7590

06/17/2002

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EXAMINER

O HARA, EILEEN B

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 06/17/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/380,276

Applicant(s)

TADA ET AL.

Examiner

Eileen B. O'Hara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 11-22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-22 ^{were} are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

1. Claims 1-22 are pending in the instant application. Claims 1, 2, 4, 5, 6 and 8 have been amended and claims 11-22 have been added as requested by Applicant in Paper Number 14, filed March 25, 2002.

Claims 9 and 10 are withdrawn as being drawn to a non-elected invention.

Claims 1-8 and 11-22 are currently under examination.

Substitute Sequence Listing

2. The substitute sequence listing has been entered as requested by Applicant.

Withdrawn Objections and Rejections

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Claim Objections

4. The objection to claim 8 is maintained and new claim 22 is also objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. Claim 8 can depend from claim 1 *or* claim 7, but not from both, and claim 22 can depend from claim 2 *or* 7, but not from both claims.

Appropriate correction is required.

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Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-8 remain rejected and new claims 11-22 are rejected under 35 U.S.C. 101

because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for reasons of record in the previous Office Action, Paper No.11 at pages 3-6.

Applicants traverse the rejection and assert that the polypeptides of the present invention possess utility based upon their membership in the TNFR family, by virtue of their source of isolation (stromal cells, which are known to produce and secrete essential factors to induce proliferation and differentiation of stem cells), and as having, for example, cell proliferating and cell differentiating activities.

In support of the asserted utility, Applicant have submitted a computerized analysis of the domain structure of the polypeptides which identifies the proteins of the present invention as comprising TNFR domains and therefore as being members of the TNFR family.

Applicants' arguments that the polypeptides have utility based upon their membership in the TNF receptor family and based upon their isolation from stromal cells have been fully considered but are not deemed persuasive. The evidence is convincing that the polypeptides are members of the TNFR family. However, the issue is that the members of this family of receptors are diverse, have different expression patterns, bind different ligands, mediate different signals and produce different responses in cell types, and therefore have different utilities, based upon these specific activities. Also, though stromal cells may produce and secrete essential factors

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that induce cell proliferation and differentiation of stem cells, one of ordinary skill in the art would not consider it to be predictive that any given factor secreted by stromal cells would have these activities. Additionally, the Eby et al. reference, discussed below, presents evidence that the protein of the instant invention is primarily expressed in testis, and thus is not expected to be a stromal stem cell differentiation factor.

Applicants submit the reference of Eby et al. as further support of the cell proliferating and cell differentiating activities of the polypeptides of the present invention. The amino acid sequence of TAJ in the Eby et al. reference is 98.5% identical to SEQ ID NO: 4 of the present invention and may therefore be a probable allelic variant (or a splice variant). Eby et al. present evidence that TAJ may be a key regulator of cell activation and death during embryonic development, and present evidence that TAJ is expressed in embryos, and in adults only in the prostate gland with only very low expression seen in other tissues such as spleen, thymus, testis, uterus, small intestine colon and peripheral blood leukocytes. Eby et al. also present experiments in which TAJ was transiently over-expressed in 293EBNA cells and activated the JNK pathway, and experiments in which transient expression of TAJ did not successfully activate the NF- κ B pathway, and experiments in which TAJ induced caspase-independent cell death, but in which it was dependent on cell type (COS cells did not undergo apoptosis). Further experiments showed that TAJ did not demonstrate nuclear fragmentation, a key feature of caspase-induced apoptosis, that the JNK pathway did not play a major role in TAJ-induced cell death, and that TAJ interacts with TRAF family members TRAF1, TRAF2, TRAF3 and TRAF5. In the discussion, Eby et al. state:

Despite sharing significant sequence homology with TNFR family members in the extracellular ligand-binding domain, TAJ possess a unique cytoplasmic domain, which

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suggests that it utilizes novel signal transduction pathways for the activation of JNK and cell death pathways.

The Eby et al. reference is evidence that the activities and functions of TAJ (SEQ ID NO: 4 of the present application) are quite different from other members of the TNFR family and need to be further elucidated, and that the protein is somehow involved in cell death, based on in vitro over expression experiments. Eby et al. support the assertion that the polypeptides are members of the TNF receptor superfamily, but its function in TRAF mediated signal transduction pathways and apoptosis were not present or envisioned in the specification as originally filed, and inducing apoptosis by over expression is not a patentable utility. There has been no demonstration made that the proteins have cell proliferating and cell differentiating activities, and there has been no nexus demonstrated between the protein and any disease or disorder. Therefore, the rejection based on 35 U.S.C. § 101 is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-8 remain rejected and new claims 11-22 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the particularly disclosed polypeptides, enablement would not be found commensurate in scope with the claims. There is no guidance to support the scope of the

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claims in the specification or the prior art, no working examples and low predictability.

Therefore, the rejection based on 35 U.S.C. § 112 first paragraph is maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

5. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner



**LORRAINE SPECTOR
PRIMARY EXAMINER**